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10/734,573	12/12/2003	Wendelin Frick	DEAV2002/0087 US NP	1865

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EXAMINER	
ISSAC, ROY P	

ART UNIT	PAPER NUMBER
1623	

NOTIFICATION DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/734,573	FRICK ET AL.	
	Examiner	Art Unit	
	Roy P. Issac	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *05 November 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12* is/are pending in the application.

4a) Of the above claim(s) *9-12* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This Office Action is in response to Applicant's amendment/ remarks/ response filed 11/05/07.

The requirement for election of species set forth in the office action dated 9/15/06 is withdrawn. Thus, claims 1-8 are examined on the merits on the full scope herein.

Rejections Withdrawn

In view of the withdrawal of election of species set forth above, and the examination of claims in their full scope, obviousness rejection set forth in the prior office action dated 5/04/07 in regards to the elected species over claims 1-8 is withdrawn.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or

patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-8 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-10 and 15 of copending Application No. 11/567,410. Although the conflicting claims are not identical, they are not patentably distinct from each other because the fluorine substituted compounds of claim 1 herein overlaps with compounds claimed in the '410 application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 8 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 8 recites, "one or more blood glucose lowering active ingredients." The specification does not include a list of compounds that fall into this category. It is not clear which of the existing compounds or which of the compounds yet to be discovered will fall into this category.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 8 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the use of one of the compounds of claim 1, does not reasonably provide enablement for a combination of a compound of claim 1 with any "one or more blood glucose-lowering active ingredients". The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The instant specification fails to provide information that would allow the skilled artisan to practice the instant invention. Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

(1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence

or absence of working examples; and (8) the quantity of experimentation necessary.

Nature of the invention and the breadth of the claims:

The instant claims are directed to a combination of a class of compounds described as "one or more blood glucose-lowering ingredients" and one of the compounds of claim 1. Since the description encompasses all known and any compounds to be developed for lowering blood-glucose the claims are considered very broad.

The relative skill of those in the art:

The relative skill of those in the art is high, with a typical practitioner having obtained a PhD, M.S. or equivalent advanced degree.

The predictability or lack thereof in the art:

It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. *In re Fisher*, 427 F.2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. In the instant case, the instant claimed invention is highly unpredictable since one skilled in the art would recognize that the recitation encompasses thousands of compositions with varying effects and unknown side effects. As such, each composition will need to be individually evaluated for activity.

The description of the class of compounds as "one or more blood glucose-lowering active ingredients" is considered a functional description. Functional language at the point of novelty, as herein employed by Applicants, is

admonished in *University of California v. Eli Lilly and Co.* 43 USPQ2d 1398 (CAFC, 1997) at 1406: stating this usage does "little more than outline goal appellants hope the recited invention achieves and the problems the invention will hopefully ameliorate". The CAFC further clearly states that "[A] written description of an invention involving a chemical genus, like a description of a chemical species, requires a precise definition, such as by structure, formula, [or] chemical name, of the claimed subject matter sufficient to distinguish it from other materials" at 1405 (emphasis added), and that "It does not define any structural features commonly possessed by members of the genus that distinguish from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the genus.." at 1406 (emphases added).

The presence or absence of working example and the amount of direction or guidance presented:

The specification does not provide any working examples of any combination of any other blood-glucose lowering drugs with any compounds of claim 1 herein. The lack of working examples is a critical and crucial factor to be considered, especially in cases involving an unpredicatable and undeveloped art. See MPEP § 2164.

The quantity of experimentation necessary:

Combination therapy, and drug-drug interactions are known in the art to have various effects, and when physicians use several drugs in combination,

they face the problem of knowing whether a specific combination in a given patient has the potential to result in an interaction, and if so, how to take advantage of the interaction if it leads to improvement in therapy or how to avoid the consequences on an interaction if they are adverse. A potential drug interaction refers to the possibility that one drug may alter the intensity of the pharmacological effects of another drug if given concurrently. The net result may be enhanced or diminished effects of one or both of the drugs, or the appearance of new effects, which is not seen with either drug alone. The frequency of significant beneficial or adverse effects is unknown. The interaction between the drugs may be pharmacokinetic, i.e. alteration of the absorption, distribution, or elimination of one drug by another, or may be pharmadynamic, i.e. interactions between agonists and antagonists at drug receptors. The most important drug-drug interactions occur with drugs that have serious toxicity and low therapeutic index, such that relatively small changes in drug level can have significant adverse consequences. Additionally, drug-drug interactions can be clinically important if the disease being controlled with the drug is serious or potentially fatal if left under treated. Drugs are known to interact at any point during their absorption, distribution, metabolism, or excretion; the result being an increase or decrease in concentration of the drug at the site of action. As individuals vary in their rates of disposition of an given drug, the magnitude of an interaction that alters pharmacokinetic parameters is not always predictable, but can be very significant. See Goodman & Gilman's: The Pharmacological Basis of Therapeutics, 10th Edition, McGraw-Hill Medical Publishing Division, 2001, pages

54-56. **Thus, the teachings of the book clearly support that the instant claimed invention, administering a** combination of a compound of claim 1 and any compound that can be considered "one or more blood glucose-lowering active ingredients" **is highly unpredictable.**

Genentech, 108 F.3d at 1366, sates that, "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion." And "patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable."

Therefore, in view of the *Wands* factors as discussed above, to practice the claimed invention herein, a person of skill in the art would have to engage in ***undue experimentation*** to practice the invention commensurate in scope with the claims.

Claim Rejections - 35 USC § 103

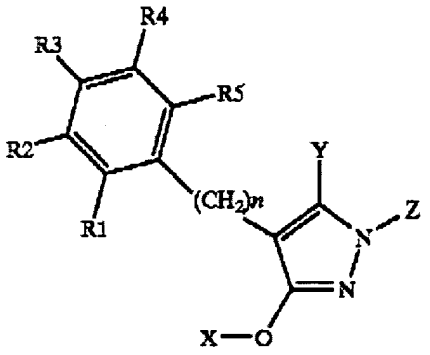
The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

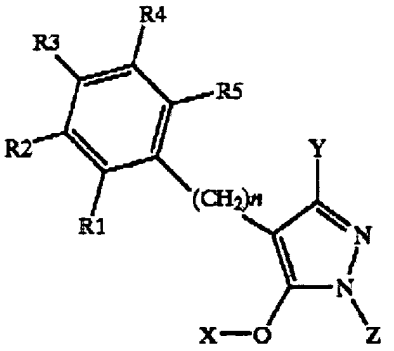
> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ohsumi et. al. (U.S. Patent No. 6,815,428; Of record) in view of Scarlett

Goon and Carolyn R. Bertozzi (Metabolic substrate engineering as a tool for glycobiology; Glycobiology, Principles, Synthesis and Applications, Chapter 18, 2001, Pages 641-674; PTO-892) further in view of Blanchard et. al. (Chemistry & Biology, 8, 2001, 627-633; Of record).

Ohsumi et. al. discloses a series of compounds with strong structural similarity to the elected species herein. (Examples 1-16, Columns 31-35, Claims 1-17). Ohsumi et. al. discloses the following compounds for the treatment of diabetes. (Column 36-37).





Note that the x moiety represents a beta-D-glucopyranosyl group as claimed herein.

Ohsumi does not disclose a compound wherein the R1 or R2 of the glucopyranosyl ring is fluorine as claimed herein.

Goon et. al. teaches the effects of halogenation on sugar moieties. Goon particularly point out the use of fluorine as the most commonly used halogen. (See pages 655-659).

Blanchard et. al. discloses that the substitution of fluorine in sugar in either C2 or C5 positions can significantly slow the metabolism of glycosides. (Page 628, Column 1, Paragraph 3 to Column 2, Paragraph 1).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to make and use the compound of the instant application because the compound is a structural analog of the compounds disclosed for the treatment of diabetes by Ohsumi et. al. and the substitution of fluorine on the sugar moiety is a well known strategy used in glyco-drugs.

One of ordinary skill in the art would have been motivated to make and use the instant compound for the treatment of diabetes because the compound is a structural analog of those disclosed in Ohsumi et. al. and the substitution of the sugar moiety with fluorine is expected to slow metabolism of the compound without sacrificing the inhibitory efficacy. Furthermore, the fluorine substituted compounds are considered structural analogs of the compounds disclosed in Ohsumi et. al.

Therefore, one of ordinary skill in the art would have reasonably expected that the substation of the sugar moiety with fluorine will result in substantially similar or better pharmaceutical efficacy.

As noted in MPEP 2144, "If such a species or subgenus is structurally similar to that claimed, its disclosure may motivate one of ordinary skill in the art to choose the claimed species or subgenus from the genus, based on the reasonable expectation that structurally similar species usually have similar properties. See, e.g., Dillon, 919 F.2d at 693, 696, 16 USPQ2d at 1901, 1904.

See also Deuel, 51 F.3d at 1558, 34 USPQ2d at 1214. The utility of such properties will normally provide some motivation to make the claimed species or subgenus. Id. Dillon, 919 F.2d at 697, 16 USPQ2d at 1904-05 (and cases cited therein). If the claimed invention and the structurally similar prior art species share any useful property, that will generally be sufficient to motivate an artisan of ordinary skill to make the claimed species, In fact, similar properties may normally be presumed when compounds are very close in structure. Dillon, 919 F.2d at 693, 696, 16 USPQ2d at 1901, 1904. See also In re Grabiak, 769 F.2d 729, 731, 226 USPQ 870, 871 (Fed. Cir. 1985) ("When chemical compounds have very close' structural similarities and similar utilities, without more a prima facie case may be made."). Thus, evidence of similar properties or evidence of any useful properties disclosed in the prior art that would be expected to be shared by the claimed invention weighs in favor of a conclusion that the claimed invention would have been obvious. Dillon, 919 F.2d at 697-98, 16 USPQ2d at 1905; In re Wilder, 563 F.2d 457, 461, 195 USPQ 426, 430 (CCPA 1977); In re Linter, 458 F.2d 1013, 1016, 173 USPQ 560, 562 (CCPA 1972).

Thus, the claimed invention as a whole is clearly prima facie obvious over the combined teachings of the prior art.

No claim is allowed. This rejection is made NON-FINAL due to the new/modified grounds of rejection.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Roy P. Issac whose telephone number is 571-272-2674. The examiner can normally be reached on 9:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia Anna Jiang can be reached on 571-272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

1/22/08

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